U.S.S.N. 09/760,046
Filed: January 12, 2001
AMENDMENT AND RESPONSE TO OFFICE ACTION

Claim 1 was amended to incorporate the limitations of canceled claims 2 and 14 and to delete "greater than 90% solid particles are less than 1 μm in diameter". Support for these amendments can be found in originally filed claims 2 and 14. Claim 1 was further amended to specify that the particles of agent are micronized in step (b). Support for this amended can be found in the specification at least at page 5, lines 5-6 and page 29, lines 14-15. New claim 27 includes the size limitation that was deleted from claim 1. Support for new claim 27 can be found in original claim 5.

Applicants believe that it is proper for the present amendment to be entered since it places the application in condition for allowance. Alternatively, entry of this amendment is proper since it places the claims in better form for appeal, does not raise any new issues, and does not require further consideration or search. Additionally, by amending claims, the claimed subject matter is narrowed since it is limited to methods for making dry micronized particles of an agent, which involve forming an emulsion in step (b) and the separation of the macromolecular material from the micronized particles of agent, in step (e).

Rejection Under 35 U.S.C. § 103

Claims 1-4 and 6-26 were rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 5,817,343 to Burke ("Burke"). Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

The claimed methods

The claims have been amended to recite that the micronization of the particles of agent occurs in step (b), as suggested by the Examiner.

The claimed methods are directed at forming micronized particles of agent, such as a drug. In the claimed method, the particles are micronized while the agent is dissolved or dispersed in solution with the matrix material (see claim 1, step (b)). After freezing and drying, the particles of agent are separated from the matrix.

Burke

Burke is limited to micronizing a matrix by fragmenting (e.g., grinding, milling) the matrix below the glass-transition point of the polymer. Burke requires the step of grinding or milling to micronize the matrix. Burke mills or grinds a matrix which contains a drug to reduce the size of the matrix particles. Therefore nowhere does Burke teach or suggest micronizing particles of drug, as required by the amended claims. Further, Burke does not teach the claimed steps for forming dry micronized particles of agent. Therefore, claims 1-4 and 6-27, as amended, are nonobvious in view of Burke.

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Allowance of claims 1-4 and 6-27, as amended, is respectfully solicited.

Respectfully submitted,

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Certificate of Facsimile Transmission

I hereby certify that this Amendment and Response to Office Action, and any documents referred to as attached therein are being facsimile transmitted on this date, February 18, 2003, to the Commissioner for Patents, U.S. Patent and Trademark Office, Washington, DC 20231.

Pam Turnbough

Date: February 18, 2003

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MARKED UP VERSION OF AMENDMENTS PURSUANT TO 37 C.F.R. § 1.121(c)(1)(ii)

Marked Up Version of Amended Claims

Pursuant to 37 C.F.R. § 1.121(c)(1)(ii)

1. (Twice Amended) A method for making dry, micronized particles of an agent, comprising:

(a) dissolving a macromolecular material in an effective amount of a solvent, to form a solution;

(b) dissolving or dispersing the agent in the solution to form [a mixture] an emulsion and thereby micronize the particles of the agent;

(c) freezing the mixture; [and]

(d) drying by vacuum the mixture to form solid [to form solid] micronized particles of the agent dispersed in solid macromolecular material[, wherein greater than 90% of the solid particles are less than 1 μm in diameter]; and

(e) separating the solid micronized particles of agent from the macromolecular material.

Please cancel claim 2.

3. (Amended) The method of claim 1 further comprising encapsulating the solid particles of agent in an encapsulating material.

4. (Amended) The method of claim 1 wherein greater than 90% solid particles are less than 0.2 μm in diameter.

6. (Amended) The method of claim 1 wherein greater than 90% of the solid particles are between 10 nm and 1 μm in diameter.

7. The method of claim 1 wherein the agent is a bioactive agent.

8. The method of claim 7 wherein the bioactive agent is a protein.

9. The method of claim 8 wherein the protein is a growth hormone.

10. The method of claim 8 wherein the protein is an osteoprotegrenin.

11. The method of claim 7 wherein the agent is selected from the group consisting of peptides, antibiotics, nucleotide molecules, and synthetic drugs.

12. The method of claim 1 wherein the macromolecular material is a polymer.

13. The method of claim 12 wherein the polymer is selected from the group consisting of polymers of lactic acid and glycolic acid, polyanhydrides, poly(ortho)esters, polyurethanes, poly(butic acid), poly(valeric acid), poly(caprolactone), poly(hydroxybutyrate), poly(lactide-co-glycolide), poly(lactide-co-caprolactone), and blends and copolymers thereof.

Please cancel claim 14.

15. The method of claim 1 wherein step (d) utilizes lyophilization.

16. The method of claim 3 wherein the encapsulation is conducting using a process selected from the group consisting of interfacial polycondensation, spray drying, hot melt microencapsulation, and phase separation techniques.

17. (Amended) The method of claim 16 wherein the phase separation technique is selected from the group consisting of solvent extraction, solvent evaporation, and phase inversion.

18. The method of claim 17 wherein the mixture has a continuous phase containing the solvent and wherein the phase inversion technique comprises:

introducing the mixture into a nonsolvent, wherein the volume ratio of solvent:nonsolvent is at least 1:40, to cause the spontaneous formation of a microencapsulated product, wherein the solvent and the nonsolvent are miscible.

19. (Amended) The method of claim 18 wherein the solvent and non-solvent are slightly miscible.

20. The method of claim 18 wherein the volume ratio of solvent:nonsolvent is between 1:50 and 1:200.

21. The method of claim 18 wherein the macromolecular material is dissolved in the solvent at a concentration of less than 10% weight per volume and wherein the mixture has a viscosity of less than 3.5 cP.

22. The method of claim 20 wherein the concentration of the macromolecular material in the solvent is between 0.5 and 5% weight per volume.

23. (Amended) The method of claim 8 wherein freezing of the mixture is performed following addition of the agent to the solution at a rate effective to avoid denaturing of the protein.

24. (Amended) The method of claim [2] 1 wherein the particles of agent are separated from the solid macromolecular material using a method comprising

dissolving the macromolecular material in an effective amount of a solvent for the macromolecular material, wherein the solvent is a nonsolvent for the agent.

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25. The method of claim 3 wherein the encapsulating material is a biocompatible polymer.

26. The method of claim 25 wherein the biocompatible polymer is selected from polyesters, polyanhydrides, polystyrenes, poly(ortho)esters, copolymers thereof, and blends thereof.

27. (New) The method of claim 1 wherein greater than 90% solid particles are less than 1 μm in diameter.